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JANUARY 1959

VOLUME XXXVI NUMBER 3

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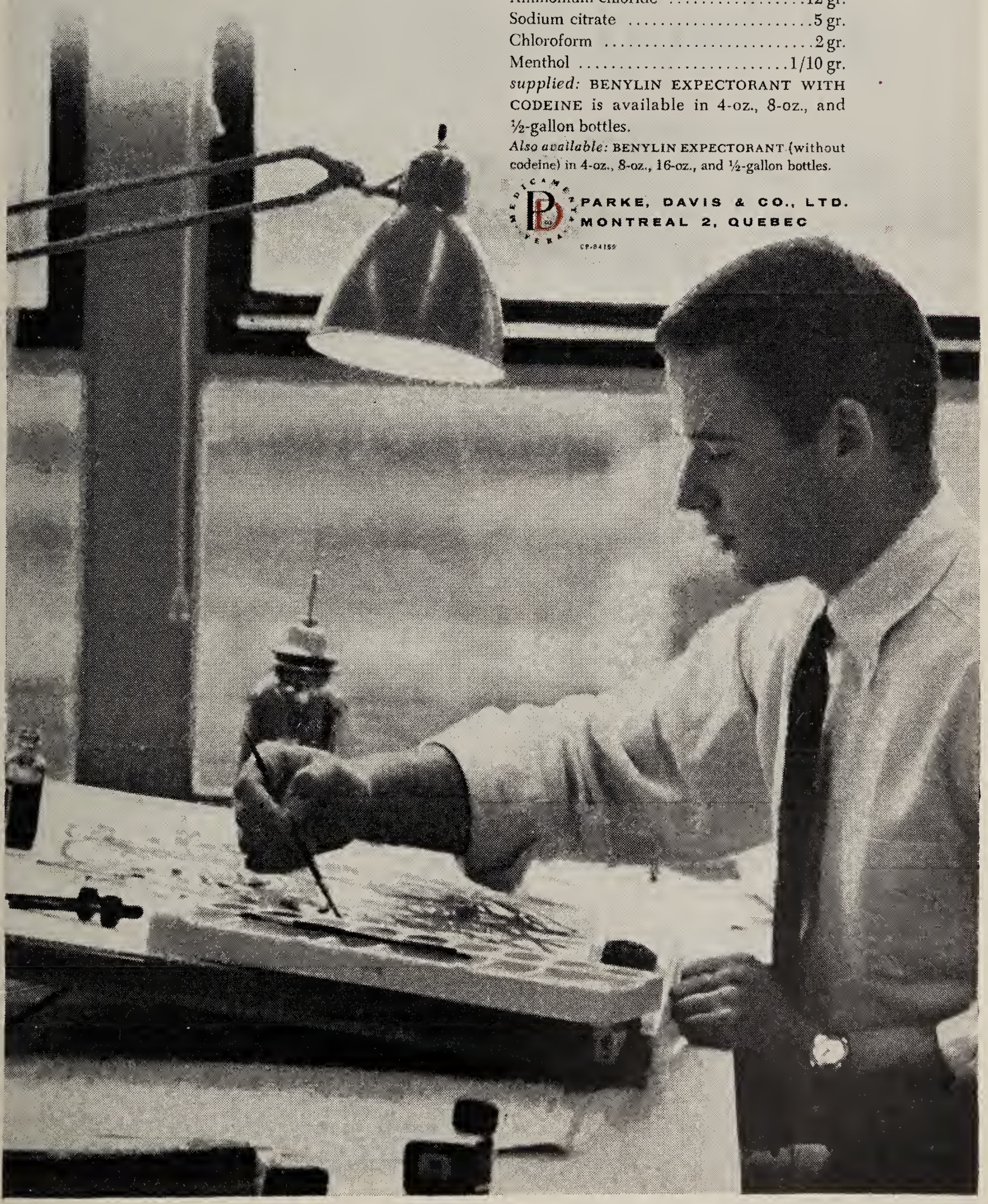

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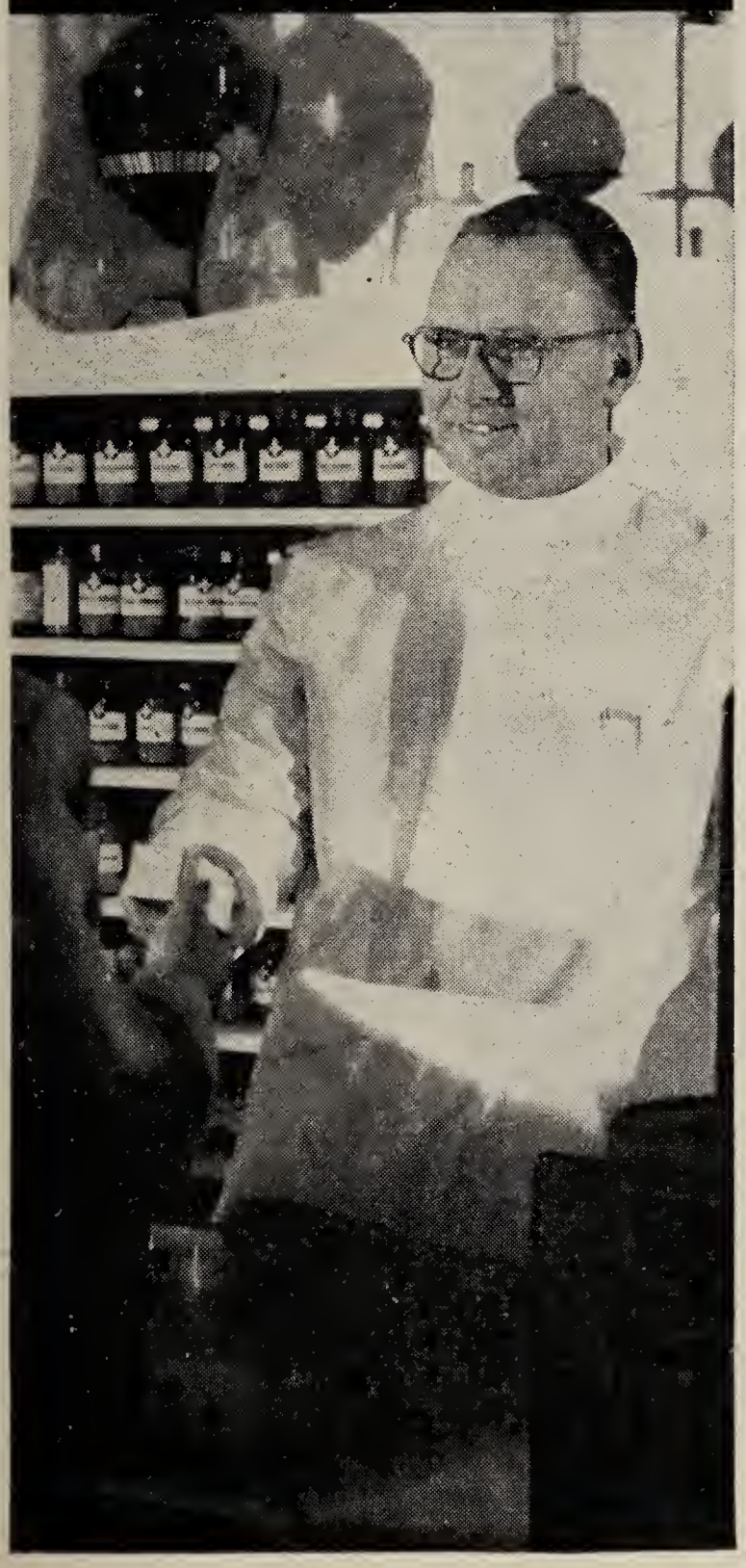

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THE CONTROL OF FERTILITY

G. W. PERKIN, 5T9

EVERY physician in the course of medical practice encounters patients who for physical or other reasons require advice on the control of fertility. The physician is the only authoritative source of contraceptive counsel and must therefore be familiar with modern methods and their clinical effectiveness.

When a patient is to receive advice on family planning, a detailed history must be taken and should include menstrual, gynecologic and obstetric history. In the physical examination a complete pelvic examination should be done to determine the presence of any anatomical abnormalities. When the method of contraception has been selected the patient must receive detailed instructions about its use, and after this demonstration she should be required to show that she knows how to follow the advice given. Three factors that will influence the method of contraception to be prescribed include—pelvic findings, the patient's ability to follow the instructions given and motivation for use. It is evident since each of the above three factors will vary from patient to patient that the physician must have available several methods from which to select the one best suited to each individual patient.

Throughout the years many devices and methods have been used to prevent conception. Some are still recommended, others have been discontinued because they are potentially dangerous, and many have not proven to be effective or acceptable. Methods which have fallen into relative disuse in this country include cervical caps, intrauterine stems and rings, sponge and powder, suppositories, radiation and surgery.

The efficacy of a method is dependent upon numerous factors such as spermicidal activity, acceptability, non irritation, convenience of use, ease of application, availability, inexpensiveness, familiarity with the technique, absence of effect on future fertility, and motivation on the part of the patient and her husband.

The purpose of this article is to give a concise presentation of acceptable contraceptive methods so that they may be prescribed effectively for the requirements of individual patients.

1. Rhythm Method

INDICATION:

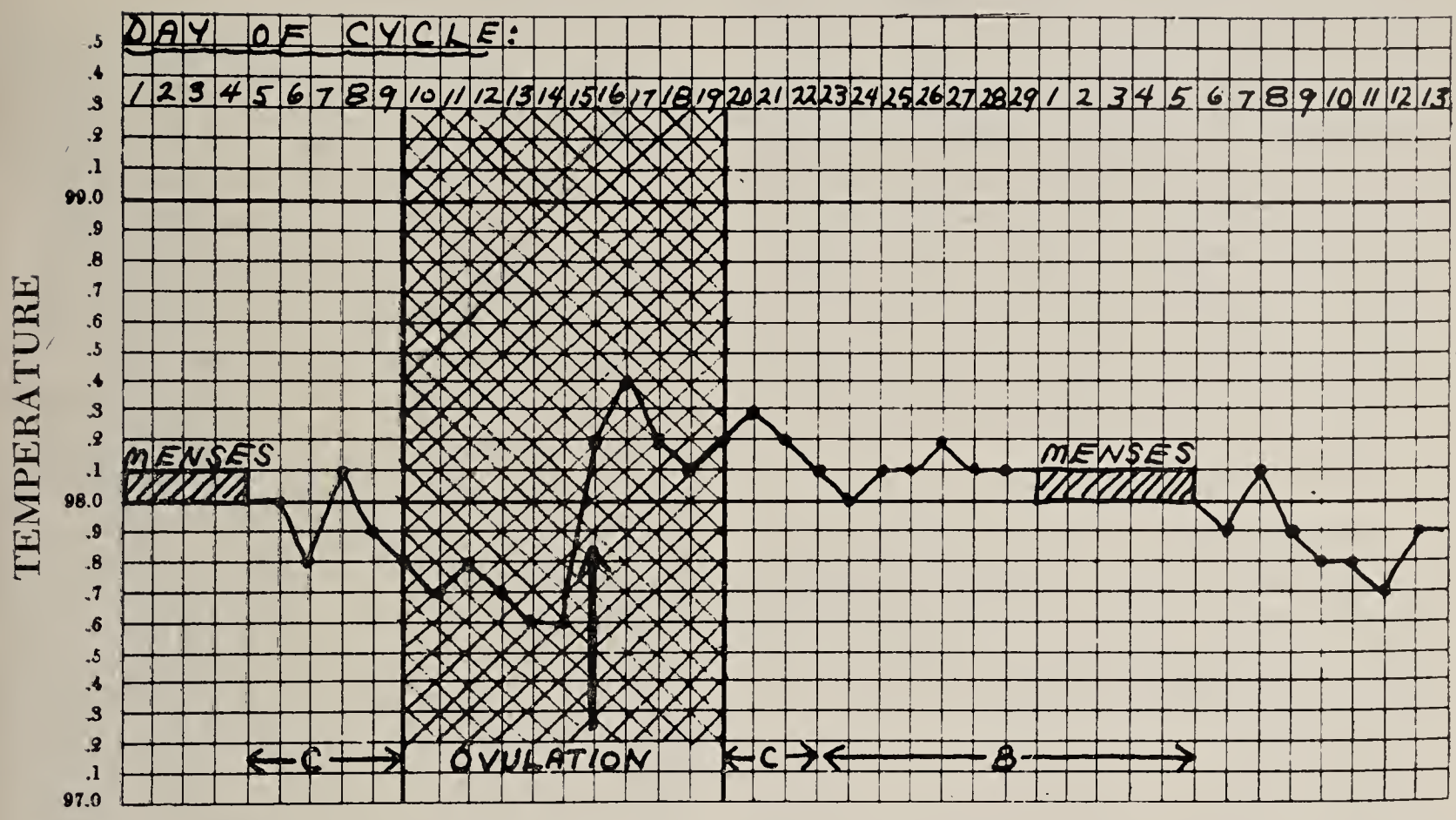
Where other methods are unacceptable due to religious or personal beliefs.

PRINCIPLE:

Following menstruation the primordial follicle in the ovary is stimulated by the follicle stimulating hormone of the anterior pituitary gland. In a patient with a twenty-eight day cycle, the developing follicle reaches maturity at approximately the fourteenth day and ovulation occurs. Conception is most likely to occur in the 24–48 hour period following ovulation. During the first half of the menstrual cycle the basal body temperature is lower than it is during the latter half, marked by a relatively sharp increase of one half to one degree about the time of ovulation. It is therefore possible to identify the probable date of ovulation by keeping a record of the body temperature from day to day. By avoiding coitus during this probable period of ovulation the chance of conception occurring is considerably reduced.

BASAL TEMPERATURE RECORD

(After Hamblen)



Shaded Area—"Fertile" Period.
B—Period of Least Chance of Conception.
C—Moderately "Safe" Period.

INSTRUCTIONS:

The patient should be instructed to take her oral temperature immediately upon awakening, before arising and prior to talking, eating, drinking or smoking. The temperature is plotted on a simple graph as shown. This graph should be repeated for at least three months and preferably for an entire year. By reference to past graphs the day of ovulation for the coming month may then be predicted. Coitus should be avoided for at least four days on either side of the probable day of ovulation. For a patient with a regular 28-day cycle this means abstinence from the tenth to the eighteenth day following the onset of the last menstrual period. The longer the period of abstinence on each side of the proposed date of ovulation the more likely is this method to provide satisfactory control of conception. In many women the cycle will vary considerably from month to month and in these patients the "safe" period will be considerably reduced.

2. Condom or Sheath

INDICATIONS

(i) Presence of infection.

(ii) Increased protection desired by combination with another method such as the applicator method.

(iii) Personal preference.

(iv) Premature ejaculation in the male. Sensation is decreased somewhat by this method.

PRINCIPLE AND INSTRUCTIONS:

The condom is designed to prevent the entry of semen into the vaginal canal. It is the most generally available of any of the more effective birth control measures, mechanical or chemical. It is relied upon

to furnish about a fifth to a fourth of the desired immunity against pregnancy in the United States.[1] This method is the least "physiological" of the modern methods and has consequently become somewhat less popular among those who are aware of the other methods available. The physician is seldom called upon to recommend this method and little, if any, instruction need be given to the patient.

3. Diaphragm and Jelly:

INDICATIONS:

The desire for adequate protection against conception in a patient who is anatomically normal, reasonably intelligent and highly motivated.

PRINCIPLE:

The occlusive diaphragm is a dome shaped, latex coated, coiled or flat spring which when in position extends from the posterior fornix of the vagina to behind the pubic symphysis. During coitus it fits closely to the anterior or upper vaginal wall thus effectively shielding the cervical opening. The patient is completely unconscious of its presence once it has been properly inserted. A spermicidal jelly or cream is applied so as to be held in contact with the cervix thus affording an effective "secondary" chemical barrier against spermatazoa entering the cervical canal. The patient must be measured for this device by means of rubber rings varying in size. It is important that the proper size in millimetres be obtained for each individual patient or adequate protection will not be afforded. Should a moderate retroversion, cystocoele, or rectocoele be present it may be impossible to obtain a satisfactory result and the selection of another method should be seriously considered. After each pregnancy or vaginal operative procedure the patient must be examined again and a new diaphragm prescribed if necessary.

INSTRUCTION:

After the correct size diaphragm has been determined and inserted by the physician, the patient is instructed to familiarize herself with its proper position by feeling how the anterior rim is lodged behind the symphysis and how the cervix is covered by the dome. Under supervision the patient should insert and remove the diaphragm. Prior to use five cubic centimetres (1 teaspoon) of a spermicidal jelly or cream is applied to the side of the diaphragm which will contact the cervix. Additional jelly may be added to the rim and reverse side if desired. The diaphragm should be left in position for at least six hours following coitus and may be placed in the vagina up to two hours prior to coitus. It must be emphasized that unless the diaphragm is used conscientiously and its proper position checked by the patient on every occasion adequate protection cannot be ensured.

COMMENT:

The common causes of failure with this method include: irregular use, use of the diaphragm without any spermicidal preparation, improper insertion, douching immediately following coitus, or removing the diaphragm immediately after coitus. The occlusive diaphragm is, however, still felt by many authorities to offer the most complete protection against conception. For many patients with only moderate motivation this will not be the case for the diaphragm will prove to be "too difficult" or "too much trouble". In cases where motivation is high the diaphragm and jelly method does offer excellent protection.

4. Applicator Method:

During the past few years as a result of research new preparations with

improved bases and more potent spermicidal substances have been developed for use without an occlusive device such as a diaphragm.

INDICATIONS:

Desire for adequate protection against conception in a patient with:

(i) Moderate motivation,

(ii) Some anatomical abnormality—retroversion, cystocoele rectocoele etc., or

(iii) Desire for a "simple" method

PRINCIPLE

Spermicidal agents in a suitable base are inserted by means of an applicator into the vagina prior to coitus. These preparations offer a "chemical" barrier to spermatazoa and thus prevent their entry into the cervical canal. Some of these preparations also offer a mechanical type barrier by their physical composition. A gel, for example, when inserted properly will occlude the cervical os and the spermicidal agent in the gel will then effect the chemical barrier. Other preparations, cream, for example, are so spermicidally effective that a mechanical barrier is not necessary to ensure protection.

INSTRUCTIONS:

The patient should be instructed to use one applicator-full of the recommended preparation prior to coitus, and to insert the applicator well back in the vagina so that the majority of the material remains in the region of the cervix. No douche is required following use, but if it is desired it must not be taken until six to eight hours after coitus. Several commercial preparations are available. Many physicians recommend all of these enabling the individual patient to decide which product is personally most acceptable.

COMMENT:

Common causes of failure of the applicator method include: irregular use, douching immediately after coitus, only using one applicator-full for several occasions, or using the preparation *after* coitus. This simpler method has nevertheless proven to provide adequate protection against conception. In selecting this method for patients it is important to consider that it is better to recommend a method which the patient is likely to use because of its simplicity rather than a more "technically" perfect method which is more difficult and is less likely to be used in each and every occasion.

5. ORAL CONTRACEPTION:

At present clinical evaluation of a synthetic steroid of the 19-nortestosterone series to which a small amount of estrogen has been added is being carried out. This product when taken for twenty days a month successfully inhibits ovulation. Withdrawal bleeding or sham menses follows discontinuing the drug after which time the medication is resumed. The long-term effect of such a preparation on the normal endocrine balance is still unknown.

CLINICAL EFFECTIVENESS:

In studying the clinical effectiveness of a contraceptive method it is necessary to distinguish between its physiological effectiveness and its use effectiveness.[5] Physiological effectiveness is defined as the effectiveness of a method under ideal conditions where omissions and errors of technique do not occur. Such ideal conditions are rarely present in any large series of cases. Physiological effectiveness is therefore not accessible to direct observation and measurement but must be higher than the degree of protection achieved by the most successful group of users. What can be observed and measured is "use effectiveness" which reflects not only the physiological effectiveness and acceptibility of the method, but also, the nature of the population using it. Use effectiveness is generally

higher among the intelligent and better educated than among the backward and underprivileged, higher in cities than in rural areas, and higher among couples who seek advice on their own initiative than among those who have been persuaded by social workers or others to attend a clinic. A common method for the study of human fertility and its control is the pregnancy rate per 100 years of exposure.[5] To compute this rate for a group of cases one first determines for each couple the duration of exposure to the risk of pregnancy by deducting from the aggregate months of married life those months during which conception was impossible because of pregnancy, separation, or the like. The months of exposure and pregnancies of all couples under observation are then added and the pregnancy rate per 100 years of exposure computed by the following formula:

$$R = \frac{\text{Total no. of conceptions} \times 12 \times 100}{\text{Total months of exposure}}$$

USE EFFECTIVENESS OF CONTRACEPTION.

Method and Author	*Bibl. No.*	*Locality of Study*	*Social Environment*	*Years of Exposure*	*Acc'l Preg.s*	*Pregnancy Rate*
Control: Without any form of contraception:						65–80
Rhythm: Tieze et al.	6	Boston	U. Cl.	606	87	14
Condom:						
Stix & Notestein	7	New York City	U. Cl.	204	13	6
Tietze & Gamble	8	North Carolina	R.	297	19	6
Stix	9	Cincinnati	U. Cl.	325	32	10
Tietze & Gamble	8	North Carolina	R.	307	49	16
Diaphragm & Jelly:						
Dewees & Beebe	10	Philadelphia	U. Pr.	935	59	6
Beals	11	New York	U. Cl.	472	32	7
Dubrow & Kuder	12	New York	U. Cl.	237	23	9.7
Garvin	13	South Carolina	M. Cl.	104	11	11
Applicator Method:						
(*a*) Stromme & Rothnem	14	Minneapolis	U. M.	337	14	4
(*b*) Tyler	16	Los Angeles	U. Cl.	506	27	5.3
(*a*) Dubrow & Kuder	12	New York	U. Cl.	310	25	8
(*b*) Dubrow & Kuder	12	New York	U. Cl.	53	3	7.6

U.—Urban
R.—Rural
Cl.—Clinic
Pr.—Private
M.—Mixed (Urban & Rural)

(*a*) Preceptin Vaginal Gel
(*b*) Delfen Vaginal Cream

The pregnancy rate per 100 years of exposure in societies where contraceptive measures are not employed is variously stated as between 65 and 80 per 100 years. This means that if a woman was fertile for one-hundred year period she would theoretically have 65–80 pregnancies. Using this method it is therefore possible to tabulate the pregnancy rate obtained with the various methods discussed (see table). The figures in the table were obtained by a survey of some of the literature over the past 20 years. It should be emphasized that the differences between groups using the same method are primarily due to differences in residence, education, degree of motivation etc. Since in no two

studies are these conditions exactly similar, comparison between the results obtained with the different methods is not statistically valid. The only valid conclusion that can be drawn from this table is that all the methods of conception control discussed will be successful in reducing the pregnancy rate by from 80–95% when prescribed to patients under clinical conditions. These results are not applicable to the success which an individual patient will obtain using any one given method. For example in the Tyler report,[16] the pregnancy rate is calculated on the basis of 27 pregnancies occurring. If these are broken down individually it is found that 6 of these patients admitted incorrect use of the method, 6 irregular use, 14 ran out of supplies, did not care if pregnancy occurred, and only one patient who became pregnant claimed constant use. If "patient" failures are excluded the effectiveness of any of these methods is thus increased greatly. For general purposes of tabulating results it is generally accepted that these "patient" failures must be included in the overall pregnancy rate.

Conclusion

In prescribing a method of conception control for an individual patient it is important not to recommend the method which may appear to be technically the most effective, but the method that that patient is most likely to find acceptable and therefore most likely to use regularly. Once this method has been selected by the physician a period of instruction and explanation is necessary to ensure the maximum effectiveness of that method. In this article the four most commonly used methods of conception control and their clinical effectiveness have been discussed. It is hoped that for further information on this topic, the reader will consult the various articles mentioned in the Bibliography.

Acknowledgement

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Bibliography

1. Dickinson, R. L.: Techniques of Conception Control: Williams & Wilkins, 1950.
2. Planned Parenthood Federation Of America: Simple Methods of Contraception, 1957.
3. Ortho: Modern Medical Methods for the Control of Conception, 1957.
4. Stopes: Contraception, 1949. Putnam.
5. Tietze C.: The Clinical Effectiveness of Contraception, Third International Conference on Planned Parenthood, 1952.
6. Tietze, Christopher et al.: The clinical effectiveness of the rhythm method of contraception: Fertility & Sterility **2**(5): 444–450, Sept. 1951.
7. Stix & Notestein: Controlled Fertility; Baltimore: Williams & Wilkins, 1940.
8. Tietze, Christopher & Gamble, Clarence J.: The condom as a contraceptive method in public health work; Human Fertility **9**(4): 97–211, Dec. 1944.
9. Stix, Regine K: Birth control in a midwestern city; Milbank Memorial Fund Quarterly **17**(1): 69–91 Jan. 1939.
10. Dewees, Lovett & Beebe, Gilbert: Contraception in private practice; J. Am. Med. Assn. **110**(15): 1169–1172 April 9, 1938.
11. Beals, Dorothy: A clinical study of diaphragm and jelly; J. Contraception **3**(4) 77–79; April 1938.
12. Dubrow, Hilliard & Kuder, Katherine: Combined postpartum and family-planning clinic; J. Obs. & Gyn. **2**(5): May 1958.
13. Garvin, O. David: Jelly alone vs. diaphragm and jelly; Human Fertility **9**(3): 73–76, Sept. 1944.
14. Stromie, William B. and Rothnem, Morris: Clinical experience with a new gel-alone method of contraception; Annals, N.Y. Acad. Sciences **54**(5) 831–840, May 1952.
15. Tyler et al.: Clinical effectiveness of a new vaginal contraceptive cream; West. J. of Surg., Obs., Gyn., **64**: 152–157, March, 1956.
16. Tyler et al.: Observation on the Clinical Use of cream-alone and gel-alone methods of Contraception; Obs. & Gyn., **10**(3), September 1957.

GOUT

A. R. COCHEN, 5T9

DEFINITION AND HISTORY:

GOUT is a hereditary constitutional disease characterized in most instances by an elevated serum uric acid level and recurrent attacks of acute arthritis. The first unequivocal evidence of gout may be traced to the first century of the Christian era. In a cemetery in Upper Egypt a skeleton was discovered whose joints showed large tophi which revealed urates on chemical analysis. The word "gout" (Latin *gutta*—a drop) was first used in the thirteenth century to indicate a disorder of joints in general i.e., a synonym for arthritis.

There are few diseases that have had such a great number of eminent men as victims as has gout. The list includes Milton, Harvey, Sydenham, Newton, Fielding, Congreve, the Pitts, Bacon, Darwin, Benjamin Franklin and others.

TERMINOLOGY:

Acute gouty arthritis is a descriptive term which refers to the acute articular episodes. The intercritical period is the interval between acute attacks during the early stages when there are no chronic progressive changes and when the patient is symptom free between the attacks. Chronic tophaceous gout occurs in only a proportion of patients, and is characterized by chronic arthritis with destruction, as a result of tophaceous deposits in cartilage and bone. Urate deposits in the form of tophi may also occur in subcutaneous tissue, bursae, tendons and kidney.

HEREDITY AND INCIDENCE:

The hereditary factor in gout had been alluded to by several early observers including Galen (A.D. 131–201) and Aurelianus Caelius, a fifth-century Roman. One series studied by Talbott revealed that one in five of the relatives of patients with gout have a significant hyperuricemia. The current thought is that the genetic transmission of the trait for hyperuricemia is due to a single dominant gene with incomplete penetrance. The proportion of females afflicted with the condition is about 5 per cent. In this connection it is interesting that the age of onset may be postpubertal in males but is almost always postmenopausal in females.

PATHOLOGY:

The cause of the inflammatory reaction in acute gouty arthritis is obscure and doubt has been cast on uric acid as being the immediate etiologic factor. The reasons for this are:

(1) in chronic tophaceous gout, in which there are large urate deposits, acute inflammatory episodes may be absent;

(2) intravenous injection of uric acid to normal and gouty patients has failed to induce an acute attack;

(3) colchicine, which specifically suppresses acute gout does not affect synthesis or excretion of uric acid while Benemid, which increases excretion of uric acid, does not affect acute gout.

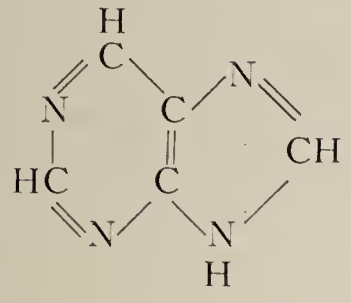
In chronic gout the urate crystals are deposited in the superficial portions of the articular cartilage, in the synovial and capsular tissues as well as the periarticular tissues, tendons and subchondral bone. The crystal deposits result in a degeneration of the articular cartilage which may lead to osteoarthritic changes, obliteration of the joint cavity by urates or chronic tophaceus synovitis. The typi-

cal tophus consists of multicentric deposits of urate crystals with a foreign body granuloma surrounding these.

Gouty nephrosis with albuminuria is usually the result of deposition of microscopic urate deposits in the renal parenchyma and especially in the pyramids. Such changes may be found in a majority of patients with long-standing gout in a benign form, but in some cases may result in more serious damage with impairment of renal function. In a small number of cases the urate deposits may cause mechanical obstruction of the tubules.

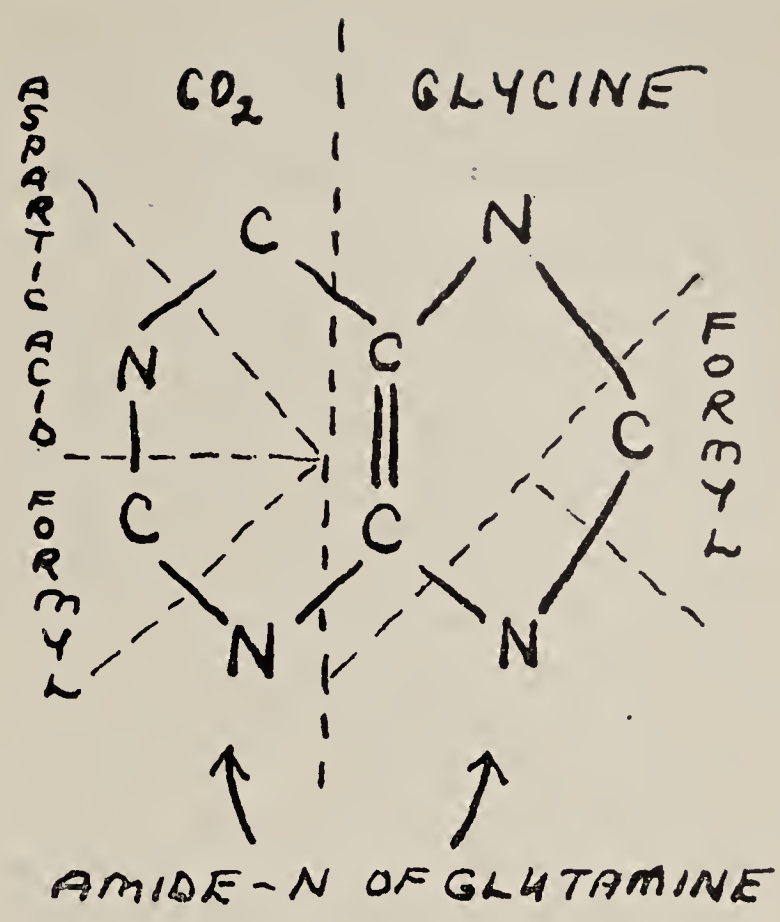
Intermediary Purine Metabolism:

All nucleoproteins on hydrolysis are split into proteins and nucleic acids and the latter can be further hydrolyzed into nitrogenous bases (purines and pyrimidines), sugar and phosphoric acid. The purines are derivatives of the following ring compound called purine by Fischer.



The purines which occur in all nucleic acids are adenine (6-amino-purine) and guanine (2-amino-6-hydroxy-purine). Hypoxanthine, xanthine and uric acid are derived from these purines by deamination and oxidation. It is now known that purines can be synthesized in the body. The following figure indicates the various precursors of the carbon and nitrogen atoms in the purine ring.

Through a series of reactions involving glycine, the first purine base inosinic acid (hypoxanthine ribotide) is formed. Inosinic acid may then be oxidized to xanthylic acid which is the immediate precursor of guanylic acid.



The formation of uric acid in man has been presumed to result from the deamination and oxidation of the purine moieties of nucleic acids. As a result of cleavage by phosphatases and phosphorylases the free purine bases adenine, guanine, hypoxanthine and xanthine are formed. Guanine is deaminated and hypoxanthine is oxidized to yield xanthine. The only established reaction generating uric acid is the oxidation of xanthine. Uric acid is largely excreted in the urine as such and may be regarded as the end product of purine metabolism in man and the ape, in whom the enzyme uricase, which oxidizes uric acid to allantoin in other mammals, does not exist.

Metabolic Defects in Gout

Primary gout is an inborn error of metabolism manifested by an "essential" or unexplained hyperuricemia, as opposed to those cases which occur secondary to other diseases such as polycythemia vera where there is an excessive degradation of nucleic acids leading to a hyperuricemia. The cause of the elevated urate concentration in patients

with primary gout must be due to a derangement in the normal balance between rates of urate formation and rates of urate excretion or destruction.

URIC ACID PRODUCTION:

The mechanism and rates of uric acid production have been studied by two techniques: the first a turnover study employing the principles of isotope dilution; the second an isotope precursor administration study evaluating the rate and extent of the conversion of the administered substance to uric acid.

The "miscible pool" of uric acid is defined as that quantity of uric acid in the body capable of mixing promptly with intravenously injected uric acid, and consequently, of diluting the isotope. In a series of normal subjects the miscible pool contained an average of 1176 mg. of uric acid. In patients suffering from gout the miscible pool was found to be increased from 2 or 3 times normal to 25 times normal, the larger pool size being found in patients with tophaceous gout.

The rate of generation of uric acid has been studied by observing the rate at which isotope appeared in uric acid when an isotopically labelled precursor was administered. When N^{15} labelled glycine was fed to normal subjects the N^{15} concentration in urinary uric acid rose to a maximum in four days and diminished gradually thereafter, indicating that isotope was derived from a large and metabolically sluggish pool of urate precursors.

In one series three gouty patients showed the same result whereas two others showed rapid rises in N^{15} concentration in uric acid to values about 3 times normal and rapid declines during the following days. This indicated an exaggeration of the rate of incorporation of dietary glycine nitrogen into uric acid in some patients. It would appear that in some gouty patients a shunt exists whereby dietary glycine nitrogen can enter the purine nucleus of uric acid more quickly than in normal man without the intervention of the nucleic acid purines. It has also been found that the subjects who exhibited increased incorporation of glycine also excreted excessive quantities of urate. Further experiments utilizing glycine-1-C^{14} and other isotopes have been done recently but the interpretation of the results have not been agreed upon. The important point is that some people with gout produce uric acid by rapid pathways without the intervention of the slower pathways involving nucleic acids. It still remains to be demonstrated whether this explanation accounts for the hyperuricemia in all patients with so-called primary gout.

With regard to the theory of decreased excretion of uric acid by gouty patients no primary defect in renal excretion of urate has thus far been proven. In fact it is now known that a significant number of people with gout excrete excessive quantities of urate. There is also some evidence that a limited degree of uricolysis does occur in mammals but the significance of this has not yet been established.

SECONDARY GOUT:

Overt gout does occur in some cases of polycythemia, myeloid metaplasia, chronic leukemia and other hematopoietic disorders. This form of gout appears to be due to an increase in the catabolism of nucleic acids. Studies of the incorporation of glycine N^{15} into uric acid revealed that there was a prolonged excretion of urinary uric acid containing N^{15}. The difference between this pattern of excretion and the one found in normal subjects or patients with primary gout lay in the exaggeration of the slower pathway.

Clinical Features:

Precipitating factors include direct trauma, infection, surgery, exposure to cold, blood loss, myocardial infarction, injection of mercurial diuretics, insulin, vitamin B_{12} and ergotamine.

The metatarsal-phalangeal joints of the great toe are the ones most commonly affected but any part of the foot, especially the tarsus, may become involved. Other joints which may be involved include the ankles, the knees, the wrists and less frequently the elbows and shoulders. Similar attacks may involve bursae such as the olecranon and the one under the Achilles tendon.

The acute attack is sudden in onset and is accompanied by signs of local inflammation with increased heat, redness and swelling, excruciating pain and local tenderness. Dilatation of surrounding superficial veins may be prominent. When the big toe is involved the site of maximum tenderness is on the medial side of the m.-p. joint and not on the ventral or dorsal aspect. At the end of an attack the involved joint may be intensely itchy and desquamation of the overlying skin may occur.

Diagnosis:

The most reliable guides in the diagnosis of acute gouty arthritis are the clinical features, an elevated serum uric acid, and the response to colchicine. Additional supportive evidence includes a positive family history, a history of a urinary calculus, and the presence of albuminuria and hypertension. If colchicine is to be used for diagnostic purposes full therapeutic doses must be given.

The differential diagnosis usually includes acute rheumatic fever, acute rheumatoid arthritis and acute septic arthritis. The response to colchicine is virtually diagnostic of acute gouty arthritis, while in acute rheumatic fever the response to full doses of salicylates is almost diagnostic.

Rheumatoid arthritis poses the greatest problem in differential diagnosis in the chronic cases. Females are more likely to be affected with rheumatoid arthritis. The hands are more susceptible in rheumatoid arthritis whereas it is the feet which are prone to involvement in gout. Osteoarthritis does not offer too great a diagnostic problem.

The presence of a leucocytosis, an increased sedimentation rate, together with systemic symptoms such as fever, malaise, headache and tachycardia make it difficult to differentiate acute gouty arthritis from an acute septic arthritis. The diagnosis may depend on the presence of a hyperuricemia and the response to colchicine.

In patients who have had the disease for twenty years or more tophi may be present most commonly in the outer ears, hands, feet, elbows and knees. These may become ulcerated and there may be a chronic chalky discharge.

Treatment:

ACUTE GOUT

The general measures for the the treatment of acute attacks of gout include rest of the affected joints, abundance of fluids and a light diet. As a long term measure a low purine, low fat diet has been advocated. Colchicine has been the drug of choice for the treatment of the acute attack. It can be administered in doses of 0.5 mg. q. 1 h. or 1 mg. q. 2 h. until the acute pain has subsided or until the onset of nausea, vomiting or diarrhea. The full therapeutic dose should not exceed 5 to 7 mg. in any one course of treatment but another course may be repeated in 24 hours. With the onset of gastrointestinal upsets 5 ml. of paregoric may be administered q. 2 h. until the symptoms are controlled.

As an alternative, acute attacks may be treated with phenylbutazone, 200 mg. three times a day for three or four days. This is equally as effective as colchicine and does not produce gastrointestinal upsets. Under certain circumstances it may be preferable to administer these drugs by injection, colchicine 3 mg. I.V., phenylbutazone 600 mg. I.M.

Chronic Gout

Probenecid (Benemid), a potent uricosuric agent, has been the mainstay in the treatment of chronic gout for the past 7 years. Probenicid, in common with other uricosuric agents, has the property of increasing uric acid excretion through the blocking effect on tubular reabsorption. The aim has been to effect a reduction of the serum uric acid to normal or near normal levels. The initial dose is 0.5–1 Gm. depending on the severity of the condition. It is often given in combination with 0.5 mg. colchicine as a prophylactic measure against recurring acute attacks. The serum uric acid level should be checked in 6 to 8 weeks and if it has not reached normal levels the dose should be increased to the limit of 2 Gm. At some later stage the colchicine may be discontinued if the patient ceases to have acute attacks in the presence of a normal uric acid level.

Phenylbutazone in daily doses of 0.6–1.0 Gm. has been found to be an effective uricosuric agent. However its salt-retaining properties and reported toxicity have precluded its use in the treatment of chronic gout. Salicylates in a daily dose of 6 to 8 Gm. have an effective uricosuric action but the gastric irritation and development of salicylism have discouraged its use.

More recently comparisons have been made between the action of several uricosuric agents. Among the drugs used were two phenylbutazone derivatives, G 25671 (thiophenylpyrazolidine) and G 28315 (sulfoxyphenylpyrazolidine, Anturan). It was found that G 25671 and G 28315 were three and six times more potent respectively than Benemid, per unit of weight. The doses of the three drugs which effected a comparable decrease in serum uric acid levels were G 25671–1 Gm., G 28315–0.5 Gm., and probenecid–3 Gm.

In some cases 1 Gm. of probenecid is effective in lowering the serum uric acid to normal limits. However, in others 2 or 3 Gm. daily are required. These larger doses sometimes cause gastro-intestinal symptoms necessitating reduction of the dose or discontinuance of the drug. G 28315 in a dose of 0.5 Gm. has thus far proven to be relatively non-toxic.

Another drug, zoxazolamine (Flexin), which has been used in the treatment of muscle spasm has been found to be an effective uricosuric agent in a daily dose of 500 to 750 mg. and appears to be about 3 to 4 times as potent as probenecid, but somewhat less effective than G 28315.

Patients who are well controlled with uricosuric agents have noted an improvement in chronic joint stiffness and pain and an increased sense of well-being. With prolonged therapy urate deposits will gradually shrink in size or may be observed to disappear entirely.

It is important to note that retention of uric acid may occur when uricosuric agents are administered in low dosage. Furthermore, it is known that small doses of salicylates, inadequate in themselves to exhibit uricosuric effect, will tend to block the uricosuric action of probenecid on the phenylbutazone derivatives. Therefore, salicylates, even in small doses, must not be administered while the patient is under treatment with the latter drugs.

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BIBLIOGRAPHY:

1. Metabolism: Symposium on Gout, May 1957.
2. M. A. OGRYZLO AND J. HARRISON: Evaluation of Uricosuric Agents in Chronic Gout—Annals of the Rheumatic Diseases Dec. 1957.
3. J. J. BURNS, T. F. YÜ: Zoxazolamine—A.J.M. Sept. 1958.
4. G. D. KERSLEY: Treatment of Gout—The Practitioner. July 1958.
5. J. H. TALBOTT: Gout—Disease a Month. May 1957.
6. E. B. REED: Zoxazolamine—New England J. Med. 258:894, 1958.
7. W. GRAHAM: The Status of Phenylbutazone in the Treatment of Rheumatic Disorders C.M.A.J. Oct. 15, 1958.
8. DUNCAN: Diseases of Metabolism, 3rd ed.
9. HARRISON: Principles of Internal Medicine, 3rd ed.

MENINGITIS IN CHILDREN

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PREAMBLE:

HIS account is merely a résumé of the most important features of a problem of vast extent. Its purpose is to provide, in abbreviated form, those matters of clinical interest and practical significance to students in medicine. It should be noted that emphasis will be laid on the bacterial meningitides, as space does not allow for more than mention of the viral infections of the central nervous system.

DEFINITION:

Meningitis is a grave infectious disease of the meninges of the central nervous system which generally results in a well-defined clinical syndrome irrespective of the micro-organism responsible.

CLASSIFICATION:

1. Acute Bacterial Meningitis:
   (i) Meningococcal
   (ii) Pneumococcal
   (iii) Influenzal
   (iv) Streptococcal, Staphylococcal, Coliform, etc.

2. Acute Aseptic Meningitis:
   (i) Non-Viral (a) External
   (b) Internal
   (ii) Viral (a) Poliomyelitis
   (b) Coxsackie
   (c) Echo
   (d) Post-infectious—mumps, etc.
   (e) Rarer causes.

3. Chronic Inflammatory Meningitis:
   (i) Chronic Basilar
   (ii) Tuberculous.

SYMPTOMATOLOGY:

History: Usually one can obtain a history of an antecedent upper respiratory infection (URI). It is next noticed that the child, in a matter of hours or days, becomes listless, drowsy, and irritable. Nausea and vomiting, central in origin, may occur, and the vomiting may be projectile in type. Diarrhoea may be a prominent symptom. A characteristic "cerebral cry" may be noted. Commonly a marked febrile reaction occurs with a temperature ranging from 103 to 106 degrees. However, in newborns and very young infants, the temperature may be normal or even sub-normal. In older children above the age of 8–10 years fever may not be so marked. In the infant the mother may notice a bulging of the

anterior fontanelle. In the older child the main complaints may be of generalized myalgia with neck stiffness and headache.

It should be noted that the first signs of meningitis may be convulsions followed by a comatose state. A good rule to follow is that all children who have a single episode of convulsions, their first, should undergo lumbar puncture.

Examination: Generally the child will appear to be drowsy and irritable, and will shun external stimuli. A peculiar staring gaze may be noted, and uncommonly, blindness may be noted. There may be various pupillary irregularities and squint may be present. The child, especially if in the younger age group, may present in a position of marked opisthotonus.

On palpation, the fontanelle is often elevated and tense in the infant. There is commonly definite nuchal rigidity. Both Kernig's sign and Brudzinski's sign may be positive, more commonly in the older infant. All these signs of meningeal irritation may be entirely absent in the newborn.

Various disorders of the central nervous system such as paralyses, paresthesias, etc. may be presenting signs. As mentioned before the child may present comatose.

There may be general signs of an infectious process such as fever, tachycardia, tachopnoea, or even severe shock. An irregular pulse and Cheyne-Stokes breathing may be especially prominent.

It should be noted that all variations of the above-mentioned symptomatology can be expected. We will now proceed to a discussion of the different kinds of meningitis as outlined in the classification.

ACUTE BACTERIAL MENINGITIS:

(i) MENINGOCOCCAL: (also known as "Spotted Fever").

Epidemiology: This is seen most commonly in northern temperate zones being both epidemic and endemic. It is either weakly infectious or else confers immunity since second attacks are uncommon.

Clinically: symptomatology as noted. There may also be petechiae and purpuric spots due to the septic emboli of an accompanying meningococcemia. This type of meningitis ranges from the mild case with a slow onset to the severe, fulminating type with adrenal hemorrhage and shock (Waterhouse-Friderichsen syndrome) followed by death.

Diagnosis is made by examination of the cerebro-spinal fluid (CSF). CSF pressure may be raised above the normal limits of 75–150 mm Hg. A cell count in the CSF of 10–10,000 cells/cu. mm., predominantly polymorphonuclear, may be noted. CSF protein will be increased while sugar and chlorides may be reduced. Gram stain of a CSF smear may reveal Gram negative diplococci, but a positive culture is needed to make diagnosis certain. Blood and throat cultures are commonly positive. The peripheral white blood cell count will be increased with a polymorphonuclear shift. As in all infections of the central nervous system urine sugar and albumin may be raised above normal limits.

Treatment: This should be treated as an emergency.

(a) Isolate and report to Public Health Dep't.

(b) An intravenous infusion should be started both to replenish water and electrolytes lost and to provide a vehicle for medication. Oral feeding should be instituted as soon as is possible. A venous "cut-down" is customary.

(c) Gantrisin (a brand of Sulfisoxazole) I.V., ⅔ gr./lb. STAT to 30 gr., and ⅓ gr./lb. to 15 gr. q. 4 h. Continue for 5 days or to recovery on clinical grounds.

(d) Penicillin I.V. (aqueous) 2,000,000

u. q. 2–4 h. When the intravenous is stopped these drugs are given P.O. and I.M. respectively for at least 7–10 days. Sulphadiazine P.O. 2 gr./lb./day q. 4 h. Procaine penicillin I.M. 800,000 u. q. 8 h.

(e) Barbiturates and paraldehyde are given to control restlessness and convulsions. Paraldehyde 1cc./10 lbs. q. 4 h. given deeply I.M. or ½ cc/10 lbs. I.V. in saline.

(f) If the Waterhouse-Friderichsen syndrome supervenes, appropriate dosages of hydrocortisone must be administered I.V. and sometimes vasoconstrictors such as levarterenol may be needed. In the severely ill case due to any cause steroids I.V. may prove beneficial.

(g) Blood transfusion and oxygen may both be of assistance. Prophylactic sulpha for contacts is advised.

Course and Prognosis: With the advent of antibiotics the mortality rate of this disease has dropped from 30% to 2%. Sequelae are also much less common. Those sequelae of importance are cranial nerve palsies, deafness, blindness, hydrocephalus, subdural effusions, and skin sloughs. Hemiplegia may also be seen. An unfavourable prognosis is anticipated with the presence of the following criteria:

1. Patient less than one year of age.
2. A fulminating variety of the disease.
3. Late institution of treatment.
4. The development of hydrocephalus.

(ii) PNEUMOCOCCAL:

Epidemiology: This is seen most commonly in infants and displays a seasonal incidence similar to that of pneumococcal pneumonia of which it may be a complication. It follows a URI and may be due to any one of the several antigenically different types of the pneumococcus.

Clinically: Generally there is less marked opisthotonus than with other types due to the fact that the exudate is more commonly collected over the cortices of the brain rather than at the base. A pneumococcal pneumonia may be present. Convulsions tend to be more common than in the other meningitides and the fontanelle bulges to extreme degrees. This may also be a fulminating type of illness.

Diagnosis: CSF pressure may be increased markedly as a spinal block may be present. The CSF may be clear at first but later becomes grossly purulent with a high cell count. Generally a high cell count with few bacteria is a better prognostic sign than a low cell count with many bacteria. Protein will be increased while sugar and chlorides may be reduced. Smear of CSF may reveal Gram positive diplococci, and culture will be positive. Throat and blood cultures are usually positive also. The peripheral white count will be increased and albumin and sugar may be present in the urine.

Treatment should be vigorous.

(a) Isolate and start an intravenous infusion by cut-down.

(b) Gantrisin as in meningococcal meningitis.

(c) Aqueous penicillin as in meningococcal meningitis.

(d) Potassium penicillin G may be given intrathecally in severe cases—10,000 u. in 10 cc. saline, slowly.

(e) Solu-cortef (hydrocortisone) 5–10 mg. has been given slowly intrathecally and is thought to be valuable in preventing fibrous organization and the formation of a spinal block.

(f) Systemic steroids, blood transfusions, barbiturates, paraldehyde and oxygen may all be required as supportive measures.

Course and Prognosis: The mortality rate is about 10–20%, and the course may be prolonged and difficult. Sequelae are common and are subdural effusions, spinal block with the development of

hydrocephalus, empyema, arthritis, and pericarditis.

(iii) INFLUENZAL:

Epidemiology: H. Influenzae Type B is almost exclusively the organism responsible. This type of meningitis is commonly seen from 6–12 months of age, being rare after four years. It invariably follows a URI.

Clinically: The general symptomatology applies here. The pathology is interesting in that there are usually loculated areas of pus over the basilar meninges and in the cortical sulci.

Diagnosis: The CSF is quite turbid and the pressure is increased. There is the typical increase in cells with a predominance of polymorphs. The electrolytes follow the usual pattern of a purulent meningitis. Smear of the CSF will show pleomorphic Gram negative bacilli. A positive culture on blood agar finalizes the diagnosis. A bacteremia commonly is present.

Treatment:

(a) Isolation and an intravenous "cut-down" should be started.

(b) Chloromycetin I.M. 25 mg./lb. q. 8 h. X 3 then q. 12 h. is the drug of choice.

(c) Gantrisin I.V. as in meningococcal meningitis.

(d) Streptomycin I.M. has also been used. Intrathecal streptomycin 25–50 mg. for one to three doses may be of value in severe cases.

(e) The aforementioned supportive measures are of assistance.

(iv) STAPHYLOCOCCAL, STREPTOCOCCAL, COLIFORM, AND OTHER RARER CAUSES:

These are generally rarer causes of meningitis in children, and are most commonly seen in conjunction with congenital abnormalities of the central nervous system or post-operatively. Streptococcal meningitis is seen most commonly in the first month of life and carries a high mortality. Generally these causes show the general symptomatology of purulent meningitis, and diagnosis rests upon differentiation by bacteriological study. It should be noted that sensitivities to antibiotics should be done upon all organisms isolated from a case of meningitis and the appropriate antibiotic instituted as soon as possible.

NOTE: Where bacteriological facilities are not available or where there will be delay in obtaining the results of bacteriological study, an immediate routine of treatment must be started with regard to antibiotics. Hence the following "Routine for the Treatment of Unknown Purulent Meningitis" as used at the Hospital for Sick Children in Toronto:

(a) Gantrisin I.V. ⅔ gr./lb. STAT to 30 gr. and ⅓ gr./lb. q. 4 h. to 15 gr.

(b) Aqueous Penicillin I.V. 2,000,000 u. q. 2–4 h.

(c) Chloromycetin I.M. 25 mg./Kg. q. 8 h. X 3 then q. 12 h. or 25 mg./lb. q. 8 h. P.O.

ACUTE ASEPTIC MENINGITIS:

The derivation of this term is of historical note in that it was originated to explain the many cases of clinical meningitis seen which apparently had sterile CSF. It has since been found that by far the majority of meningitides originally included in this group are viral in origin. However, the author includes this main heading in the classification since he feels it is still useful, especially for diagnostic purposes.

(i) NON-VIRAL:

(a) *External*: This is a clinical meningitis due to exogenous irritation and not a primary infection of the meninges.

Etiology: The causes here are many. Irritation of the meninges by contiguous infections such as mastoiditis, sinusitis, otitis media, etc. is probably the most

common cause. Others to bear in mind are thromboses, hematomas, toxins, poisonings such as with lead, and allergic responses.

Clinically: The symptomatology of meningitis generally applies here, but is of á much less marked degree. Physical examination may reveal associated findings which will make the diagnosis clear.

Diagnosis: The CSF will be clear and the pressure most likely normal. Protein and electrolytes may be slightly abnormal. The cell count is usually in the range of 50–300 cells/cu. mm. with a lymphocytic response. Smear and culture will be negative for organisms. Skull X-rays, and radiological study of the sinuses and mastoids often reveal the true diagnosis.

Treatment is of the primary disorder. Supportive therapy may have to be instituted for fever, electrolyte disturbances, etc.

Course and Prognosis is relative to the cause except in the case of contiguous infection where extension may occur with a resultant true bacterial meningitis.

(b) *Internal*:

Etiology: Many infectious agents which do not reveal themselves on ordinary culture media. Included are syphilis, leptospirosis, toxoplasmosis, trichinosis, and other still rarer infectious agents.

Clinical: The CSF presents the same picture as with external non-viral meningitis. Associated findings such as jaundice, nephritis, chorioretinitis, and positive agglutination tests will aid in the diagnosis of leptospirosis. Positive serology will aid with syphilis. A peripheral blood eosinophilia will aid with the diagnosis of parasitic infestations. Culture of CSF on special media may reveal the organism responsible.

Treatment is specific for the agent responsible. Supportive therapy may be required.

Course and Prognosis is relative to the infecting agent.

(ii) VIRAL:

(*a*) *Poliomyelitis*: It is impossible to give an adequate account of this disease here. Suffice it to say that it may give a typical picture of aseptic meningitis with a lymphocytic CSF response, nuchal rigidity, and all the other manifestations.

(b) *Coxsackie*: This is one of the most common causes of the acute aseptic meningitis syndrome seen to-day. A recent epidemic in Toronto has been shown due to Coxsackie B5.

(c) *ECHO*: These viruses, especially types 4, 6, and 9, rank with the viruses of poliomyelitis and coxsackie as the most common causes of this syndrome. Generally with these three viral infections there is a mild symptomatology of meningitis plus abdominal pain, diarrhoea, myalgia and a sore throat. Recently in Toronto several cases of clinical meningitis in combination with a maculopapular skin eruption and a petechial rash of the palms of the hand and soles of the feet during the acute phase have been reported. In all of the cases the virus of the ECHO group has been isolated. Recovery in 4–10 days has been the rule with no sequelae. As with any viral infection the peripheral white blood cell count ranges around normal. The CSF pressure may be increased, protein is increased while sugar and chlorides are normal. There are usually 50–300 cells/cu. mm. found in the CSF, lymphocytic in nature. The viruses may be isolated from blood, stool, and CSF. Treatment is symptomatic and expectant.

(d) *Post-infectious*: After mumps, measles, and other exanthemata a meningo-encephalitic syndrome may be seen. Usually that with mumps occurs with the onset of the mumps itself. Those menin-

gitides of measles which occur with the actual onset of measles are usually relatively benign while those which occur while the exanthem is waning are very serious. For the latter cases massive doses of systemic steroids have been found recently to be specifically valuable.

(e) *Rarer causes*: Meningitis, meningoencephalitis, and encephalitis may be due to Herpes Zoster and Simplex, Eastern and Western Equine viruses, the virus of St. Louis encephalitis and a host of others. A specific disease called Lymphocytic Choriomeningitis, benign in nature, may cause the acute aseptic syndrome.

Chronic Inflammatory Meningitis:

(i) chronic basilar:

This may be due to an insidious meningococcal infection or may be the result of an undertreated acute meningococcal meningitis. Mild signs and symptoms of meningitis may be seen. This is really a sterile inflammation of the meninges, and is very prone to fibrous organization with resultant hydrocephalus. Treatment is surgical and is quite unsatisfactory. This is rarely seen nowadays.

(ii) tuberculous:

Epidemiology: This is seen more commonly in the winter months and early spring, and is often noted after another infection such as measles, has subsided. It is usually associated with active pulmonary tuberculosis, following it by a few months. The peak occurrence of tuberculous meningitis is in the first three years of life and the Negro and Eskimo races seem to be especially prone.

Clinically: It may be said that this type of meningitis follows the discharge of tubercle bacilli from a contiguous focus of infection such as a tuberculoma, but this is at variance with those who believe the cause to be a bacteremia. Signs and symptoms may be lacking until the final stages of the disease. Generally the course may be divided into three stages:

1. *Prodromal*: Here there is irritation of the meninges. Onset is slow with a low-grade fever, drowsiness, insomnia, and the general signs of meningitis to a mild degree.

2. *Transitional*: This is the stage of increased intra-cranial pressure. Convulsions may occur, the patient is markedly drowsy and the general signs of meningitis increase in severity.

3. *Terminal*: Here there is paralysis and coma. The pupils are dilated and irregular, there is loss of the corneal reflex, the pulse is irregular, and Cheyne-Stokes breathing supervenes. The temperature may rise steadily to 106–107 degrees with loss of the heat-regulating mechanisms of the brain. Sixth nerve palsies are commonly seen.

The course from onset of initial symptoms to diagnosis is usually two to three weeks but may be prolonged. The onset may be atypical with sudden hemiparesis, convulsions, coma, etc. and this is more prone to occur in infants. On ophthalmoscopic examination the disc is seen to be chalk-white and tubercles may be seen in the choroid. Commonly the diagnosis is missed in the early stages, and this is unfortunate in that early diagnosis is *essential* for a good prognosis. Vomiting may be the only symptom.

Diagnosis: A positive skin reaction to Old Tuberculin and a positive chest X-ray are supportive evidence. Late in the disease, skin sensitivity to Old Tuberculin may be lost. A moderate leukocytosis may be seen in the peripheral blood. The CSF may be clear or may present a "ground-glass" appearance. The CSF pressure will be raised, often to very high levels. The CSF protein will be increased markedly, while sugar will be decreased and chloride values are invariably below 700 mg.% (normal being

700–750 mg.%). If a test-tube of CSF is left overnight to stand a pellicle will form, and smears from this with appropriate stain will reveal the typical acid-fast bacilli. Culture and guinea-pig inoculation complete the diagnosis.

Treatment:

(a) Bed rest for at least one year.

(b) Lumbar puncture daily for one week then as often as is required to maintain a normal CSF pressure. This is usually twice weekly for one month then monthly. Ventricular drainage may be life-saving.

(c) Streptomycin I.M. 0.5 Gm. b.i.d. for three months then every second or third day for another three months.

(d) Isoniazid (INH) P.O. 10 mg./Kg./day in two doses for three months. Then 5 mg./Kg./day to the end of 8 months, then 2.5 mg./Kg./day to 18 months. It is now thought that this drug alone may be all that is needed.

(e) Supportive therapy for a comatose state, such as correction of electrolyte disturbances is of special importance in this type of meningitis. Usually the findings are a constant alkalosis with a high potassium level and depressed Na and Cl values.

(f) The efficacy of systemic and intrathecal steroid therapy to prevent the formation of a spinal block is in question.

Course and Prognosis: The child is treated invariably for one year and improvement can be expected up to this time. Those children who are cured are much better in 3–6 months. With the advent of INH and Streptomycin the gloomy outlook of tuberculous meningitis has all but vanished. Sequelae are much less common and the mortality rate is now about 10%.

Conclusion:

The author has presented a discussion of meningitis as it is particularly applicable to children. Emphasis has been placed on the bacterial meningitides, at the expense of an adequate discussion of the viral types. However, it is in the realm of bacterial infections of the nervous system that medicine has specific therapy to offer at this time, and it is hoped that the emphasis has not been misplaced.

Acknowledgement:

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Bibliography:

Mitchell-Nelson—Textbook of Paediatrics, 1950.

Frank R. Ford—Diseases of the Nervous System in Infancy, Childhood, and Adolescence, 1952.

Paterson and McCreary—Pediatrics, 1956.

Silverthorne—Principal Infectious Diseases of Childhood, 1958.

Anglin, C. S.—Article pp. 313–322, Pediatric Clinics of North America, May, 1958.

Boyd, Gladys—Tuberculous Meningitis in Children, A. M. A. Journal of Diseases of Children, Vol. 91, May, 1956.

Hospital for Sick Children—Manual.

CLUBBED FINGERS AND HYPERTROPHIC OSTEOARTHROPATHY

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Introduction

EVER since the latter part of the nineteenth century when von Bamberger and Marie described clubbed fingers in association with pulmonary disease,[1, 2] clinical research has shed light on the pathological definition of clubbing and hypertrophic osteoarthropathy, associated it with a variety of disease states other than those of pulmonary origin, and through experimental work has helped to establish a pathogenesis of this clinical condition. There has been renewed interest in "clubbing" due to the relationship that it bears to intrathoracic malignancy.

Pathological Definition

Clubbing is defined as a painless uniform enlargement confined to the terminal segments of the fingers and toes[4] revealing an increase in fibrous tissue, hyperemia, edema, and a mild chronic inflammation involving all layers in varying degree from the epidermis to the periosteum.[5]

Hypertrophic osteoarthropathy involves the deposition of newly formed bone in the more proximal parts of the extremities, occasionally symptomatic of a joint disorder. The local change is that of a low grade inflammatory reaction in the periosteum which is followed by a remarkable degree of periosteal new bone formation with centrifugal displacement of the thickened periosteum. The rapidity of these changes largely determines the presence of symptomatology. This bilaterally symmetrical process affects the distal third of the bones of the forearm and leg. Irregular progression occurs toward the proximal ends of these bones. The lower ends of the femur and humerus are involved in a later stage with the metacarpals and metatarsals involved in a full-blown case.[5]

These two separate processes accompany one another with hypertrophic osteoarthropathy being an extension of clubbing.[4] The one noteworthy exception is the clubbing found in cyanotic congenital heart disease.

Clubbing in cyanotic heart disease infrequently shows radiological evidence of bone changes,[6] and is not associated with a local increase in fibrous tissue.[7] The essential change in the finger tip in the "congenital cyanotic" group is that of venous pooling[9] which can be demonstrated by squeezing of the distal finger segment with the hand in the elevated position and noting the decrease in size of the finger tip.

Clinical Considerations

A. classification:

Clubbing may be classified into three types, namely the bilaterally symmetrical group, the unilateral group, and the unidigital group. This classification found in Mendlowicz's review[4] lists and discusses a wide variety of diseases in which clubbed fingers have been found. It is the author's purpose here to mention some of these conditions and not to list all disease states associated with clubbing.

Briefly, unilateral and unidigital clubbing defines local pathology. For example, unilateral clubbing is found in aneurysmal dilatation of the arch of the aorta, innominate, and subclavian artery; apical tuberculosis; apical carcinoma; and subluxation of the shoulder. Unidigital

clubbing is found in local finger trauma, median nerve injury, and felons. Boeck's sarcoid and tophaceous gout, may produce unidigital clubbing.

The bilaterally symmetrical group of clubbing falls into four categories—pulmonary, cardiac, gastrointestinal, and miscellaneous.

The pulmonary conditions giving rise to clubbed fingers are of two general types—chronic inflammatory conditions and neoplasms. The former are suppurative conditions (bronchiectasis, pulmonary abscess, and empyema) and those of diffuse pneumonitis (chronic pneumonitis, pneumoconioses—with or without Ayerza's syndrome, the pulmonary mycoses) and others (hydatid cyst, selected aortic aneurysms). Clubbing is rare in pulmonary tuberculosis and acute lung disease. It occurs in emphysema when associated with bronchitis or bronchiectasis. Clubbing is very uncommon in metastatic malignancy of the lung but is well recognized as occurring in primary malignancy of the lung or pleura.[10–24]

2. Congenital heart disease may give rise to clubbed fingers. This will be the case in cyanotic conditions, and when found in acyanotic states, bronchiectasis, or bacterial endocarditis should be considered. It occurs in acquired heart disease, in subacute bacterial endocarditis and probably due to pulmonary inflammation.[4]

3. The gastrointestinal conditions giving rise to clubbing are those of chronic diarrheal states (chronic ulcerative colitis, bacillary dysentery, amoebic dysentery, regional ileitis, sprue), obstructive lesions (pyloric, esophageal), and cirrhosis, particularly biliary or toxic types.

4. Miscellaneous. One endocrine disease associated with clubbing is the occasional case of thyrotoxicosis, or the thyrotoxic case following thyroidectomy. Hereditary clubbing[34] accounts for 3–5% of all osteoarthropathy. It occurs chiefly in males, has its onset at puberty, and often shows a familial incidence. It may become aggravated with the onset of essential hypertension.[4]

B. Signs and Symptoms:

"The earliest sign in finger clubbing is an increase in the fluctuation of the nail bed. This is rapidly followed by a thickening of the fibro-elastic tissue at the base of the nail resulting in a filling out of the angle between the nail and the basal tissues." (When the finger is in the flexed position and the normal angle of 15° is obliterated, clubbing may be said to exist).[4] "The nail bed then appears pink and shiny while the skin is stretched over the area obliterating the normal creases. Alteration in the curvature of the nail in the sagittal and coronal planes then occurs with an associated increase in the longitudinal ridging. The nails become more brittle and grow more quickly. The cuticle increases its rate of growth and keeps pace with the nail; the lunula becomes obliterated by the rapidly growing cuticle. Later, there is hyperplasia of the soft tissue in the pulp of the finger tips causing the fingers to have a typical bulbous appearance."[9]

Clubbing is rarely accompanied by symptoms. A feeling of warmth, excessive sweating or a burning sensation may accompany changes in the terminal phalanx. Hypertrophic osteoarthropathy is often asymptomatic especially in its earliest phase, being only detectable by X-ray. The bone changes may appear 6 months to 20 years after the onset of the underlying disease[4] but it is in the later stages that symptoms and signs may appear. These findings are aching pain and tenderness along the shafts of the long bones and about the joints. There may be moderate joint effusions and some limitation of movement. Awkwardness and clumsiness in hand and finger movement

may become apparent. Other manifestations are muscular weakness and skin changes (slight edema and hypertrophy of subcutaneous tissue, local hyperhidrosis, burning sensation and skin thickening, pigmentary changes, eczematoid lesions, and increase in hair growth).

In many cases where clubbed fingers are found sufficient symptomatology of the underlying disease is manifest to make recognition more or less of academic interest. Three possible exceptions to this rule are bronchiectasis, subacute bacterial endocarditis, and intrathoracic neoplasms.[4]

C. INTRATHORACIC NEOPLASMS

It has become well recognized in recent years that clubbed fingers and especially the symptomatology of osteoarthropathy may precede the pulmonary symptoms of a primary malignancy of the lung or pleura.[6, 9, 10–24] It is in these instances that bone and joint symptoms are a prominent feature. The patient shows an acute arthritis commonly affecting the ankle and knee joint initially and then progressing to involve other major and minor joints. The bone pain is deep seated, burning, and frequently aggravated by lowering of the extremities.[21] Other inflammatory signs are redness, warmth, hard pitting edema, and intense tenderness on passive movement. Since the symptoms of osteoarthropathy may often be distressing and frequently are the presenting complaint of the patient, the term acute pulmonary osteoarthropathy has been suggested[20] to draw attention to the joint picture, indistinguishable from rheumatoid arthritis, occurring in primary pulmonary neoplasms. Clubbing is almost invariably found in such circumstances and tends to be locally progressive as well. Other accompanying features are a furrowed ("acromegaloid") facies[6, 25, 13] gynecomastia,[6, 25] prominent thickening of the wrist and ankle,[6, 17, 21] and a burning sensation of the hands and feet.[6, 17]

There are many interesting aspects of the relationship of lung cancer to this syndrome. Some of these are listed below:

(1) Frequency: 5 to 10% of cases of lung cancer are associated with symptomatic osteoarthropathy.[9, 23, 20, 27] As low a figure as 2%,[16] and as high as 50%[11] have been recorded.

(2) Symptoms and signs: The features of osteoarthropathy may precede the chest symptoms by 1–57 months.[6, 21] In a study of 24 consecutive cases of symptomatic osteoarthropathy with lung malignancy, all had symptoms for 3–16 months before the mass was suspected.[7] An increase in the erythrocyte sedimentation rate would appear to be a common accompaniment of this Syndrome.[6, 9, 28]

(3) Characteristics of the tumour: Bronchogenic carcinoma (epidermoid) predominates over adenocarcinoma.[7, 20] The tumour may be less than 2 cm. in size,[20] but often is a soft bulky mass. A large series of cases[7, 20] reveal infection and/or necrosis evident on cut section[7] or absence of these changes.[20] Rapidly growing oat cell carcinoma does not produce the syndrome under discussion.[7] The lung tumour is peripheral in location in the large majority of cases.[17, 26, 22, 20, 6, 29, 30] The characteristics of the tumour should be kept in mind, for bronchoscopic examination, examination of bronchial washings and even X-ray of the chest may fail to reveal the existence of a pulmonary neoplasm.

4. Response to surgical treatment of the tumour: Because of the size of the tumour, its peripheral location, and especially since the chest symptoms lag behind the bone and joint involvement, it has been felt that such cases allow for adequate surgical removal of the underlying tumour.[20, 6, 21] The findings of osteoarthropathy and clubbing are as

important in pleural tumours, where extrathoracic symptoms are the chief clinical manifestations and where characteristic roentgen findings in the chest are wanting to allow accurate diagnosis.[19]

The other striking feature is that the bone and joint symptoms, which may be quite distressing, commonly disappear within 24 hours after tumour removal and the signs of clubbing are found to regress in periods of weeks or months. The distressing bone and joint symptoms may regress following vagus section,[27] or hilar neurectomy,[10] however clubbing does not regress.

D. PATHOGENESIS:

The response to surgical treatment has tended to support the current assumed pathogenesis of clubbing and osteoarthropathy, much of which is based on reproducable experimental evidence.[7, 31] Briefly, any condition in which the pulmonary circulation is increased without a corresponding increase in the demand for blood in the systemic circulation promotes the development of clubbing. Such a situation may result from arterio-venous anastamotic channels in the lung parenchyma. Such shunts (precapillary anastamoses) have been demonstrated in many pulmonary conditions giving clubbing and are confined to the lobe involved by the disease[32, 33] This may be the essential change occurring in the lung that explains the many disease states that give rise to the condition under consideration.[33] The current theory is that the precapillary anastamoses tend to deviate the bronchial artery blood flow. This results in ischemia of the peripheral nerve fibres of the lungs. This reflexly influences the formation of systemic arterio-venous anastamoses in the limbs through the peripheral sympathetic system. Such an increase in blood outflow due to arterio-venous anastamoses in the fingers has been established in the course of disease and post mortem.[35, 36, 37, 38] Similar changes in the bones have been inferred.[31] Thus the vascular changes in the fingers, and to a lesser extent in the bones, have been demonstrated. The initiating mechanism, however, lacks sufficient experimental evidence at present.[7] Vascular studies of resected lungs and the effect of an autonomic block, among other factors, will afford worthwhile information to evaluate the present supposed mechanism of development of the interesting condition of clubbed fingers and hypertrophic osteoarthropathy.

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BIBLIOGRAPHY

1. Wien. klin. Wchnschr. *2*, 226, 1889.
2. Zlschr. f. klin. Med. *18*, 193, 1891.
3. Rev. de Med. *10*, 1, 1890.
4. Medicine *21*, 269, 1942.
5. Am. J. Path. *27*, 349, 1951.
6. Arch. Int. Med. *99*, 431, 1957.
7. Br. Med. J. *1*, 145, 1924.
8. Clin. Sc. *9*, 299, 1950.
9. Edinburgh M. J. *56*, 655, 1949.
10. Acta Med. Scand. Supp. *266*, 467, 1952.
11. Rev. de la Assoc. Med. Argentina *62*, 690, 1948.
12. Lancet *1*, 260, 1956.
13. Geriatrics *9*, 319, 1954.
14. Dis. of Chest *16*, 483, 1949.
15. J. Thorac. Surgery *9*, 495, 1940.
16. Br. Med. J. *1*, 750, 1937.
17. J.A.M.A. *146*, 783, 1951.
18. N. E. J. Med. *233*, 18, 1945.
19. J. Thor. Surg. *24*, 213, 1952.
20. Ann. Int. Med. *38*, 239, 1953.
21. Ann. J. Med. *18*, 51, 1955.
22. Am. J. Roentgen. *60*, 232, 1948.
23. Dis. of Chest *13*, 658, 1949.
24. C. M A. J. *56*, 70, 1947.
25. Bronchogenic Carcinoma and Adenoma (Bried, B. M.), Baltimore, 1948.
26. J. Thor. Surg. *9*, 495, 1940.
27. Lancet *1*, 260, 1956.
28. Annales d'Oto-laryngologie *71*, 295, 1954.

29. Ann. Rheum. Dis. *9*, 169, 1950.
30. Ann. Int. Med. *29*, 361, 1948.
31. The Digital Circulation (Mendlowicz, M.), Grune and Stratton, 1954.
32. Thorax, *8*, 152, 1954.
33. Thorax *12*, 313, 1957.
34. Radiology *50*, 581, 1948.
35. Am. J. Roentgenol, *55*, 325, 1946.
36. Clin. Sc. *9*, 59, 1950.
37. Quart. J. Med. *21*, 201, 1952.
38. J. Clin. Inv. *20*, 113, 1941.

PRIAPISM

M. J. PORTER, 5T9

APPROXIMATELY 2,500 years ago the citizens of Lampsaeus sacrificed an ass to Priapus, the local god of fertility whose symbol was the phallus. The cult spread rapidly and widely through the civilised world of that time but the Greeks, as they began to outgrow the crudely naturalistic worships, regarded Priapus less seriously. They adopted him as the god of gardens, where a statue of a misshapen little man with large genitals stood for all to behold. Notable writers of the day dedicated several poems to Priapus but they were regarded as so obscene that they have been adequately and successfully supressed over the subsequent 2,000 years.

What is priapism? It has been defined as a sustained pathological erection of the penis unaccompanied by sexual desire. Some authorities add an anatomical limitation to this definition by confining the pathology to the corpora cavernosa. Others include erection of the corpora cavernosa, corpora spongiosum and glans as being legitimate priapisms and this view seems more logical. However, it is a fact that in most cases of priapism only the corpora cavernosa are involved, leaving the spongiosum and glans flaccid. An analogous situation has been reported in the female clitoris.

Diagnosis requires little in the way of clinical acumen. The lesion literally stares one in the face. The problem lies in determining the etiology, which varies from hanging by the neck to direct trauma as reported in Italian racing cyclists. A working etiological classification has been provided by Bailey.

A. Nervous

1) *Traumatic.* Hanging a persón by the neck usually results in priapism. This fact has been little recorded in the literature, but a French army surgeon, Marcel Guyon on the island of Martinique in 1823 witnessed 14 hangings in one day, and reported priapisms at the moment of hanging and which persisted in a semi-erect position for at least one hour. Lesions of the spinal cord, especially fracture dislocation of the cervical vertebrae, are occasionally complicated by priapism which in this case is usually of the ¾ variety and associated with urinary retention. This type of priapism is usually painless and tends to improve as paralysis improves.

2) *Organic disease.* In this category probably the commonest lesion giving rise to this condition is multiple sclerosis, but it may also be caused by syphilis. Cerebellar disease, either traumatic or vascular, will give rise to priapism and in a series of 11 cerebellar haemorrhages collected by Serres, 6 of them had priapism as part of their symptomatology.

3) *Poisoning by Aphrodisiacs.* Cantharide and Yohimbine poisoning are two rare causes. Yohimbine poisoning is interesting in that it produces the only

type of priapism in which the corpora spongiosum is more involved than the corpora cavernosa.

B. Vascular

1) *Primary phlebothrombosis.*

2) *Secondary phlebothrombosis* due to leukemia and sickle cell anaemia.

3) *Local injury.*

4) *Atherosclerosis.*

The vascular group is by far the most important group both from a primary and a secondary point of view. It is believed that clotting begins behind the erector muscles in the formed veins which connect the venous honeycomb of the phallus and the pelvic plexus and it is the clotting process which maintains the erection and not contraction of the erector muscles, as was felt by some authors. No matter the etiology, if a priapism is maintained for two days, there will be some thrombus formation in the corpora cavernosa and this will aid in maintaining the erection.

The usual cause of priapism, although of unknown origin is thrombosis of the deep dorsal veins. This is substantiated by the fact that 5 out of 6 priapisms are confined to the corpora cavernosa. When the corpora spongiosum and the glans are involved, it is indicative of a more widespread thrombotic process involving the venae profundae.

Although always cited in the literature, priapism as an adjunct to leukemia is a relatively rare event and the relation is not clearly understood. The same remarks may be applied to the combination of sickle cell anaemia and priapism. In both cases, a defect of the clotting mechanism may be involved.

Thrombosis and hematoma due to direct trauma has been reported, usually as a sudden blow. In a case of a 13 year old boy being kicked in the perineum, the lad developed lower abdominal pain, vomiting and 24 hours later, a full blown priapism with associated dysuria. Sustained trauma has been reported in Italian cyclists as giving rise to priapism.

Atherosclerosis as a cause of this remarkable condition is very rare and records in the literature are scanty.

C. Neoplastic

1) *Benign.* Prostatic hypertrophy has been cited as a cause, but priapism is an infrequent accompanient of prostatic hyperplasia.

2) *Malignant.* a) Primary. Hinman in his analysis of 170 cases noted that only two were due to primary neoplastic infiltration of the penis.

b) In the same study by Hinman there were no cases quoted as due to metastatic spread. However an analysis of two series published since then shows the primary site in 35 cases of priapism due to metastatic carcinoma as follows, bladder 10, prostate 8, rectum 7, testes 4, kidney 4, and urethra 2.

D. Psychiatric

Priapism is a purely physical condition and there are no primary psychogenic causes. However, one should be aware of the possibility of hypererotic-ism and distinguish between this and priapism.

Clinical Pictures

The striking feature of this condition is the erect penis, which maintains an acute angle to the pubis. Associated with this is a variable amount of pain. It may be so intense as to require narcotics or there may be no pain. Some authors feel that the pain is proportionate to the amount of rigidity present but the general consensus of opinion is that this is not necessarily so. Dysuria and retention of urine are not as frequent as may be imagined because of the noninvolvement of the corpora spongiosum. However some difficulty in micturition and

dysuria may be encountered in cases of pure cavernosa involvement. Age is not an important factor; it ranges from adolescence to extreme old age with a peak incidence in the twenties. Depending on the etiology there may be further clinical findings such as an enlarged spleen and abnormal blood picture in the case of leukemia, but usually there will be no further evidence of disease on examination of the patient.

Case Presentations:

During the past summer I was fortunate to see the consequences of one priapism and to be able to follow another more typical case.

1. *Case of Mr. B. H. aged 75 yrs.*

In the period between Feb. 20th and early Sept. 1958 this man had a rather remarkable medical history. He presented himself to a doctor complaining of pruritis ani, urinary frequency, dysuria and heartburn, the initial complaint being due to remaining tags of a hemorrhoidectomy and the latter considered to have little significance. Physical examination revealed a man with marked emphysema and associated polycythemia, mild essential hypertension which had not changed in the course of a year, a small right inguinal hernia, and an enlarged prostate. On Mar. 12th. a transurethral resection was performed and 26 gms. of prostate was removed, the patient making a good post-operative recovery, being discharged on Mar. 24th. with no nocturia, good stream and perfect control.

On April 7th. the patient returned complaining of extreme dysuria, hematuria and pyuria for 5 days. He had excruciating pain at the tip of the penis following micturition. The following day cystoscopy was performed and revealed a large slough at the prostato-vesical junction. A large part of the slough was removed during cystoscopy, and total removal was achieved by administering buccal varidase, the rest of the slough passing out on the 4th day of this regimen, thus relieving the patient of dysuria but leaving him with some residual nocturia and difficulty in control.

On the 14th of April he was told he was fit enough to go home but before being able to do so, a massive pulmonary infarction occurred. The blood pressure became unrecordable. He was started on I.V. levophed at 60 drops/min. using 2 vials of levophed per litre. The blood pressure was maintained at 100 systolic and it was felt by the third day that he would pull through. At the time of the infarction the patient was also started on Heparin/Dicumarol which by the 18th of April achieved a prothrombin time of 39 secs. He was kept on a maintenance dose of 100 mgms. of Dicumarol per day.

On the 18th of April the patient developed a thrombotic leg and consequently received a dose of 200 mgms. of Dicumarol on that day. In the early hours of the 19th of April the patient rang for the orderly because he was unable to pass his water. The orderly discovered the penis swollen, called the doctor, who, seeing the patient at 3:30 a.m., diagnosed priapism.

Examination revealed that the whole penis was involved, i.e., corpus cavernosa, spongiosum and glans. At this time a wide bore aspirating needle was put into each corpora cavernosa, and 5 c.c. of blood aspirated with difficulty. The blood was thick, black and viscid, clotting immediately on expulsion from the syringe despite a prothrombin time of 39 secs. Following the aspiration 150 units of Hyaluronidase was injected into each corpus in the hope of producing some disseminating effect. Gr. ¼ of Morphine was given for pain.

On the 19th of April the patient re-

ceived a further 200 mgms. of Dicumarol. By midday there was no improvement and the glans was grossly congested and showing signs of subepithelial vesication. By evening the penis was evidently becoming gangrenous and the relatively conservative measures being pursued were obviously of no avail. To complicate the picture the patient had a massive gastrointestinal haemorrhage in the evening resulting in withdrawal of all anticoagulant therapy.

On the morning of the 20th of April the penis was amputated through a racquet-shaped incision which circled the base of the penis and split the scrotum. The procedure was relatively easy, there being almost no bleeding. The urethra was brought out onto the perineum and the urethral mucosa stitched to skin. The crura of the corpora were stripped off close to the pubic rami and oversewn to control possible bleeding. The scrotum was stitched up and an indwelling catheter left in. The patient survived.

Following this the patient had a protracted convalescence complicated by the development of pneumonia, low grade osteomyelitis of the left inferior pubic ramus which fortunately cleared up on Erythromycin, periods of incontinence and dysuria, and last but not least, delirium. Amazingly, the patient began to recover about the middle of July, the powers of urinary control returning along with an increasing ability to cerebrate. By 20th. Aug. his condition had returned to the point that he was able to leave hospital with good urinary control and as a reasonably happy citizen.

2. *Case of Mr. M. B. aged 42 yrs.*

This patient presented himself at the hospital on the 1st of August having had a persistent priapism for one week. He had delayed this long because of a previous history of this condition, but finally the social embarrassment became so great that he was forced to consult a doctor.

His history began in 1955 when he had periods of erection on 3 or 4 occasions through the summer, lasting for 2 or 3 hours at a time. This history repeated itself in 1956 and 1957, in the latter year there again being 3 or 4 occasions during the summer when this condition occurred, but the priapism persisted for 5 or 6 hours, rather longer than before. Priapism arose twice during the early summer of 1958, lasting for about 3 hours on each occasion. On both occasions the priapism was relieved by a bowel movement. On the 24th of July there was recurrence, but this time there was no relief on moving the bowels, and the priapism persisted with no evidence of subsidence until admission to hospital. Along with the erection he complained of irritation of the glans, but there was no pain and no alteration of urinary function.

Complete physical examination revealed nothing except an erect turgid penis, the turgidity involving only the corpora cavernosa. Two extensive neurological examinations were negative and the rectal examination was likewise. Laboratory work on the 1st of August produced a negative urinalysis, a W.B.C. of 16,900, and a differential which had a predominance of polymorphs (82%), but no other abnormalities. Blood work 4 days later gave a W.B.C. of 10,050 with a normal differential.

A diagnosis of thrombosis of the venous plexus was made and the patient was begun on anticoagulant therapy immediately by administering 100 mgms. Danilone b.i.d. on the 2nd of August. The dose of Danilone was juggled over the next few days without obtaining a satisfactory prothrombin time until the 7th day. Also over this period he was given Chloromycetin 250 mgms. t.i.d. in

"the face" of the increased W.B.C. This was discontinued on the 10th day.

Up to the 13th day of anticoagulant therapy there was no obvious clinical improvement. The patient however claimed that he was feeling better and that his penis became softer after micturition. On the 14th day of anticoagulant therapy, which in actual fact was only the 7th day of effective treatment, there was a marked clinical improvement with an obvious and marked decrease in volume and turgidity. The patient was delighted. Anticoagulants were continued for a further 7 days at an effective level, his condition improving to the point where he could be discharged. However even on this date, the 22nd of August, the penis had not returned completely to normal, but still presented with some turgidity in the cavernosa.

Discussion of the Two Cases:

These two cases illustrate several points about priapism which have already been raised. From an anatomical and etiological standpoint Mr. M. B., the second case, is typical. Only the corpora cavernosa was involved, there was no interference with urinary function, no pain, and eventually the priapism subsided. As in most cases of priapism, the underlying etiology was unknown, although a thrombosis was suspected as the immediate cause, the blood picture substantiating this. The atypical feature of this case was the peculiar history of multiple priapisms which one author has called chronic intermittent priapism and has attributed to nerve irritation arising either from the C.N.S. or from local lesions. There were no C.N.S. or local findings in this case, but it is interesting to note that on all previous occasions the priapism had been relieved by a bowel movement, and it is unlikely that on these occasions a thrombosis was involved, whereas in the most recent manifestation there can be little doubt there was a vascular phenomenon.

In contrast, Mr. B.H., the first case, presented with a priapism which involved the whole penis and was thus indicative of a more widespread type of thrombotic lesion. There was a great deal of pain and an inability to micturate. The whole picture developed rapidly despite the usual modes of treatment being applied promptly and despite a prothrombin time of 39 secs., to the point where one of the complications set in. The commonest complications are abscess formation, cellulitis and gangrene which in this case precipitated surgical intervention.

Treatment of Priapism

On the 11th of March, 1824 Thomas Calloway treated a 4 day old priapism by applying 12 leeches, cold lotions, nauseating doses of tartar emetic, tobacco enemata and a whole range of narcotics with no success. On the 16th day of the priapism Calloway took a knife and incised the left crus below the scrotum releasing dark grumous blood clots. The patient recovered but remained impotent, a common sequel to priapism. Twenty years later in 1844, a seaman developed a priapism in the port of London. It was treated medically, unsuccessfully, and the seaman sailed for Calcutta. He returned later to report that it had spontaneously deturgesced after three months at sea. He reported impotence.

These two cases illustrate first, that after 134 years incision of the penis remains a principal method of treatment, secondly, most priapisms deturgesce spontaneously if left, and thirdly, that impotence usually follows deturgescence. Actually, it is the power of erection that is lost, the ability to ejaculate remaining.

Treatment of priapism is a controversial subject. Complete physical examination will reveal any underlying cause, and this should obviously be treated, although relief of the priapism may or may not ensue. If the etiology remains

undetermined or treatment of the cause fails to relieve it, then there is a limited choice of treatment. Adopting a logical approach, a low spinal anaesthetic is the most sensible initial step. If the priapism is of neurogenic origin then there will be immediate relief. If it is of non-neurogenic origin then nothing has been lost, and one establishes that one is dealing with a vascular condition and can proceed accordingly.

Surgical intervention remains the surest and best method of dealing with a persistent priapism. There are two approaches:

(1) Aspiration of the corpora cavernosa. This should be attempted before incision and for best results is performed in the first 48 hours. A large bore needle is put into the shaft of the right cavernosa, and repeated injections and aspiration of either saline or citrate solution is carried out. The needle can then be pushed through the septum and the same procedure carried out on the left side. Partial or complete deflation may be obtained and the penis is then firmly bandaged. It may be necessary to repeat the procedure.

(2) Incision of the corpora cavernosa. This should be carried out if aspiration fails or the priapism has been present for several days. An incision of at least one half an inch should be made to penetrate to the centre of the crus, behind the middle of the shaft of the penis. A drain is left in and antibiotics given locally and systemically to prevent infection and gangrene. This procedure will relieve priapism.

Other surgical methods such as dividing the pudendal nerve, dividing the ischiocavernosus muscle, and ligating the dorsal artery have been used but one is strongly recommended not to use them.

The advent of anticoagulants enabled medical men to attempt to treat this condition non-surgically. Their success is doubtful. Workers in Sweden were among the first to try this approach and claimed good results. Reports since that time have been variable: some claim success, some admit failure. In this light, it is interesting to note the two cases presented in this article. In the case of Mr. B. H. priapism developed while he was on anticoagulants for another condition. With Mr. M. B., the priapism persisted for almost a month, and half of this time he was on effective anticoagulant therapy. The feeling was that the priapism deflated not because of the anticoagulants but rather in spite of them. In evaluating anticoagulant therapy it must be remembered that most priapisms undergo deturgescence if left alone and if therapy is continued long enough, it will be given credit for a natural process. Most cases cited where anticoagulants have been given credit, have had protracted periods of therapy, beyond the time when they might be expected to be effective. There is also the question of what one hopes to achieve. There is no rationale for anticoagulants as a cure, only as a prophylatic measure within the first 48 hours in an attempt to prevent the blood in the corpora cavernosa from organizing and to prevent spread of the thrombus, in which case Heparin should be used. The action of anticoagulants is to limit thrombus formation; once it is present they are of little value.

A more rational medical approach is the use of an enzymatic preparation, but at present so few cases have been treated this way that it is not possible to make an evaluation. Further work is needed along this line. Mr. B. H. had a small dose of Hyaluronidase without apparent effect, but this can hardly be considered a fair trial.

Other treatments have been advocated and tried with little avail. Brody, Lahr and Caroll treated one patient by heparinizing him for 4 days, following this by forcibly massaging the penis under

general anaesthetic. This was executed for 10 minutes, the penis becoming blue and flaccid. 5,000 units of Varidase q. 6 h. for 4 days finished the cure and the patient was discharged with a semi-firm corpora cavernosa and impotent. There would appear to be little advantage in this method of approach.

Summary

Priapism is a pathological erection of the penis, usually involving only the corpora cavernosa. There is a varied etiology but in the majority of cases it remains undetermined. As far as relief, a low spinal anaesthetic should be attempted, and if this fails surgical intervention remains the treatment of choice. There is no rationale for anti-coagulants as a possible cure. Their role is in the first 48 hours, to prevent extension of the thrombotic process and to prevent blood in the corpora from organizing. The use of enzyme preparations has not been evaluated, but is logical and might be tried as an alternative to surgery. Finally, most cases of priapism will undergo spontaneous deturgescence if left long enough.

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Bibliography:

1. Bailey, H. Br. Journ. Surg. Jan. 1948, p. 298–303.
2. Bailey, H., and Matheson, N. M. Recent Advances in G.U. Surgery.
3. Berard, L. N. and Byrne, J. F. J. of Urology: vol. 70, no. 2, Aug. 1953.
4. Brody, Lahr and Carroll. J. of Urology: vol. 78, no. 2, Aug. 1957.
5. Campbell, J. H. and Cummins, S. D. J. of Urology: vol. 66, no. 5, Nov. 1951.
6. Fraser, W. J. Br. Med. Journ. no. 4936, 13th Aug. 1955.
7. Hinman. Annals of Surgery. 1914.
8. Keen. Text of Surgery. 1914.
9. Keyes. Surgical Diseases of G.U. System.
10. Lewis and Schwarz. U.S. Armed Serv. Journ. 8(2). Feb. 1957.
11. Smith, K. H. Journ. of Urol: vol. 64, no. 2, Aug. 1950.

BOOK REVIEWS

Principle Infectious Diseases of Childhood. Nelles Silverthorne, M.B.

This recent monograph prepared by Dr. Silverthorne, who is Associate Professor of Paediatrics at the University of Toronto, is a concise and complete survey of this most important aspect of paediatrics. It is divided into five distinct sections: Infections in the Newborn, Infectious or Communicable Diseases, Infection of the Nervous System, Virus Diseases, and Respiratory Infections (Non-virus). In each section the important diseases are discussed fully under the usual headings, viz. etiology, clinical aspects, complications, diagnosis, prognosis, prophylaxis, and treatment, while the less common and therefore less important diseases are described and their treatment set forth. The features that commend this book are many. It is concise and comprehensive not wasting space with extraneous and scholarly detail but rather placing emphasis on important points. It is written from clinical observations and experience, rather than purely as a textbook and hence makes for very easy reading. Perhaps the fact that it may be read in one sitting commends it to the attention of the medical student. In conclusion this work should prove to be of value

to both the student and the general practitioner.

P.B.D.

102 pages; price $3.95. Publisher—U. of T. Press.

THE ORGANIC PSYCHOSES: A guide to diagnosis. J. G. Dewan and W. B. Spaulding—165 pages. University of Toronto Press—$5.95

This monograph endeavours to present an up-to-date, complete yet concise account of diagnostic data, concerning a somewhat neglected nevertheless important field of psychiatric medicine.

The cerebral cell is used as the primary focus of attention by outlining briefly its physiological relationships. A well-organized comprehensive aetiological classification expands these first principles and is followed by short descriptions of the various illnesses as they present themselves clinically. Numerous metabolic and vascular disorders, mechanical stresses, infections, intoxications, degenerations and paroxysmal dysrhythmias are discussed with reference to physical findings, history and mental status. No exemplative case histories are imposed.

A clinical investigative approach is offered along with diagnostic orientation explaining the three categories of organic psychoses: delirium, dementia and functional mental illness associated with physical disease. The earlier classification is then fitted into these clinical groupings. Descriptive case histories, brief and well-chosen are admitted as the mode of expression in this portion. A tabled outline of useful technical procedures in diagnosis completes the work.

The authors emphasize the need for early and precise diagnosis of an organic basis in mental illness. Oftentimes a patient presenting with seemingly functional symptoms has operating organic factors which the unaware physician will neglect or augment in his management of the case. One example is an unwitnessed traumatic brain injury in a known alcoholic. Mental symptoms will confuse a medical diagnosis but with a knowledge of this subject they will more often strengthen or point to it. Thus such knowledge is imperative even to those outside psychiatry.

The Organic Psychoses is a text-book without graphs, animal experiments or statistical analysis. As a guide packed with fact it is surprisingly readable and is an invaluable reference book for its owner.

L. E. SOPER

ABSTRACTS

SOME INTERRELATIONS BETWEEN SLEEP AND DISEASE: Eugene D. Robin, A.M.A. Archives of Internal Medicine, 102: 669, 1958.

This article gives examples of how some diseases may be affected by the physiological changes associated with sleep.

1. *The Basic Nature of Sleep*: Recent investigation has suggested the concept that sleep is the normal state and the activation of "waking" centres in the brain produces the waking state.

2. *Ventilation*: While sleeping a normal person shows a rise of 5 mm. Hg. in the alveolar CO_2 tension. A subject with chronic pulmonary disease has even a greater increase which may result in a significant impairment of arterial oxygenation.

3. *Cardiovascular Function*: Changing from the upright to the reclining position causes changes in hemodynamics so that the plasma volume and pulmonary circulation increase. If left ventricular disease is present, this increase may be sufficient to cause pulmonary edema with paroxysmal nocturnal dyspnea.

4. *Adrenal Function*: There is an increase in adrenal cortical activity at night. Thus the effectiveness of steroid therapy depends upon the time of day it is administered.

5. *Red Cell Metabolism*: In paroxysmal nocturnal hemoglobinuria the hemoglobinuria is increased or only present while sleeping.

6. *Host-Parasite Relationship*: In Filariasis, the Wucheria bancrofti is most likely found in the blood at night.

7. *Blood Sugar*: While asleep normal individuals show little change in blood sugar levels while diabetics show wide variations.

R.F.A.

DEMETHYLCHLORTETRACYCLINE: A NEW TETRACYCLINE ANTIBIOTIC THAT YIELDS GREATER AND MORE SUSTAINED ANTIBACTERIAL ACTIVITY: Calvin M. Cunin and Maxwell Finland, The New England Journal of Medicine, 259: 999, 1958.

A new tetracycline antibiotic, 7-chloro-6-demethylchloro-tetracycline (DMCT), was studied in comparison with tetracycline hydrochloride.

After a single dose of 500 mg. the serum antibacterial level of tetracycline was highest for the first four hours. Thereafter the level of DMCT was higher, and with repeated oral doses the level of DMCT continued to be significantly higher. The serum level of DMCT also dropped less quickly as it is not as rapidly excreted by the kidney.

This investigation indicates that the demethylchlorotetracycline produces a higher and better sustained level of serum antibacterial activity than tetracycline.

R.F.A.

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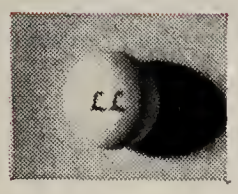
every  antibiotic

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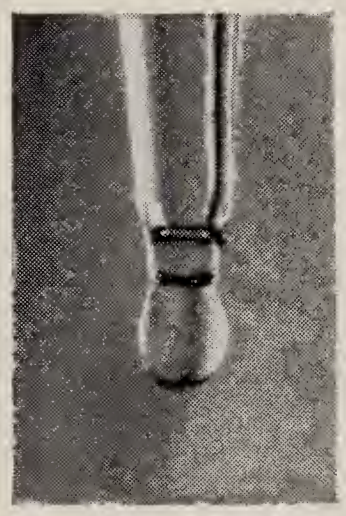

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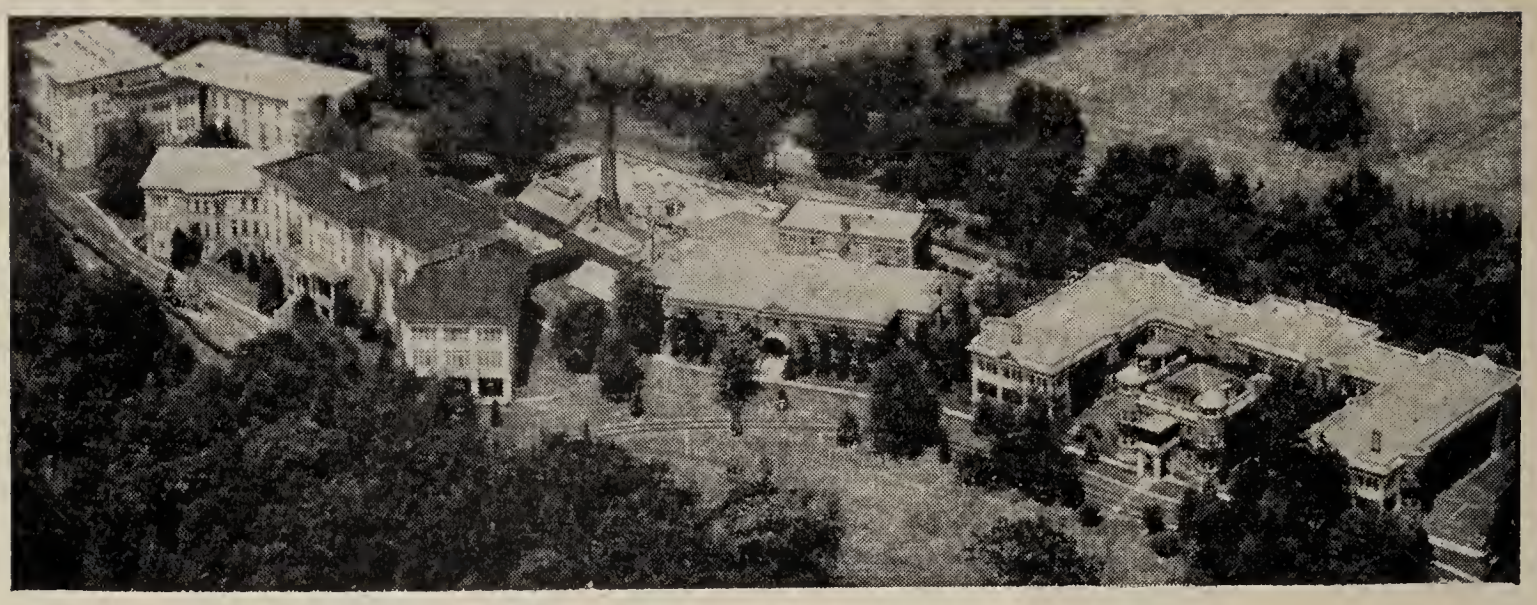

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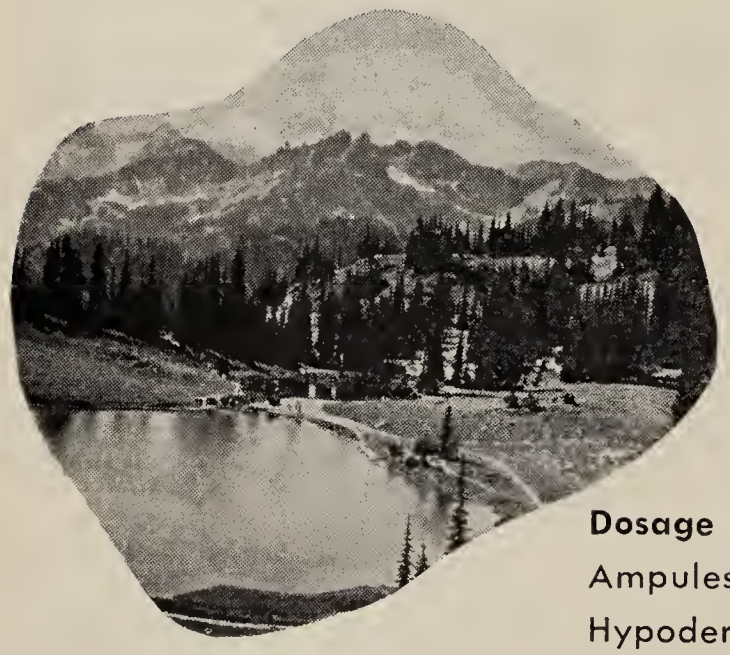

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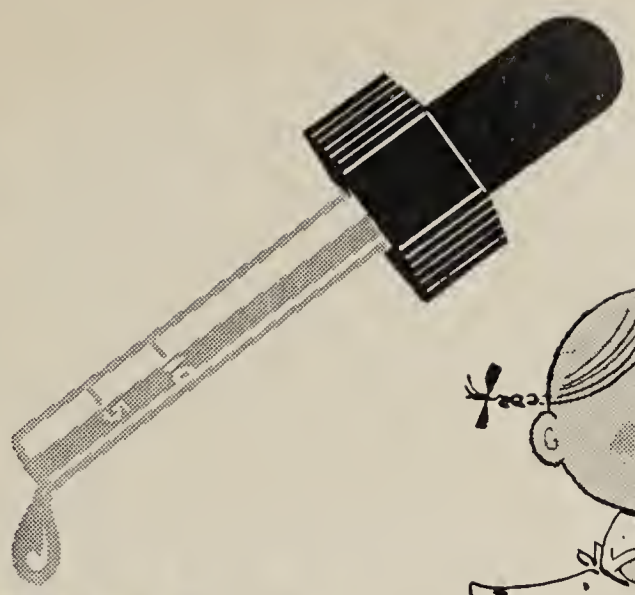

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